How to Critically Appraise a Published Study

(With an Emphasis on Feet – With Thanks to Fran Game)

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When Reading a Paper

- A few things to keep in mind
  - What is the study question (Is it clear?)
  - Is the question relevant? (Does it matter?)
  - Is there a pre-defined hypothesis?
  - Was the study design appropriate?
  - Is the study population defined and described?
  - Did the methods address sources of potential bias? (e.g. Funders)
  - Was the intervention described? Randomisation described?
  - Sufficiently powered?

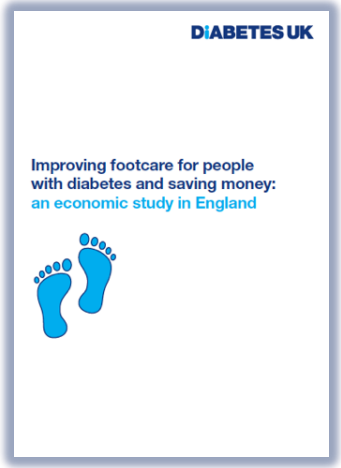
When Reading a Paper

- Continued
  - Was the study ethical (ethical approval?) (e.g. Wegener)
  - Was the study conducted as in the original protocol?
  - Was the correct statistical analysis performed?
  - Limitations described?
  - Do the results justify the conclusions?
  - Was it peer reviewed?
  - Are the results generalisable?

Why Would you Want to Do Foot Research?

	Estimated annual cost
Primary, community and outpatient care, ulceration	£629,161,354 – £786,451,692
Inpatient care, amputation	£43,797,632
Inpatient care, ulceration	£278,452,386
Post-amputation care	£20,813,777
Total	£972,225,149 – £1,129,515,487

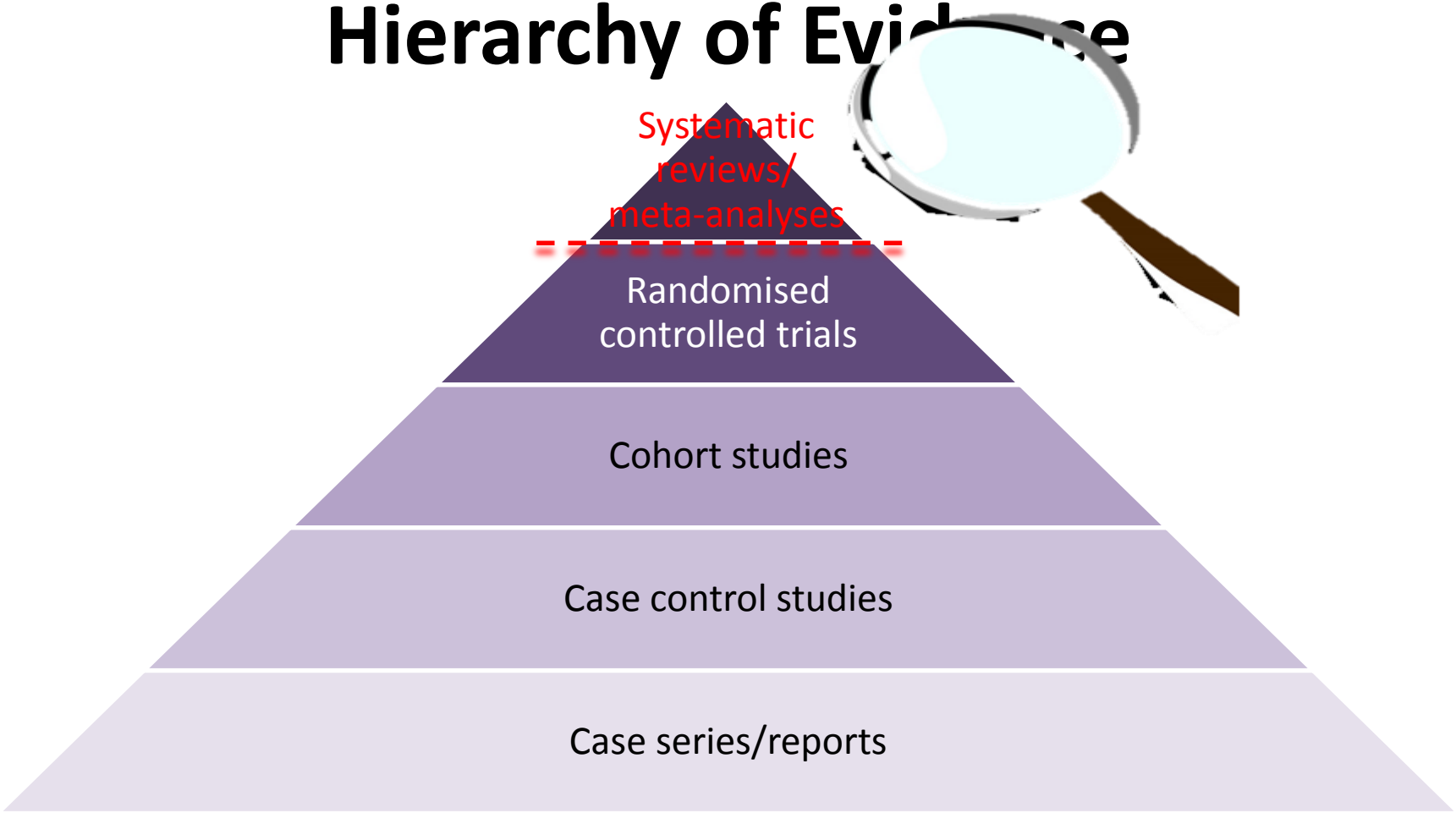
Table 1: Total estimated expenditure on diabetic foot disease, England, 2014–2015



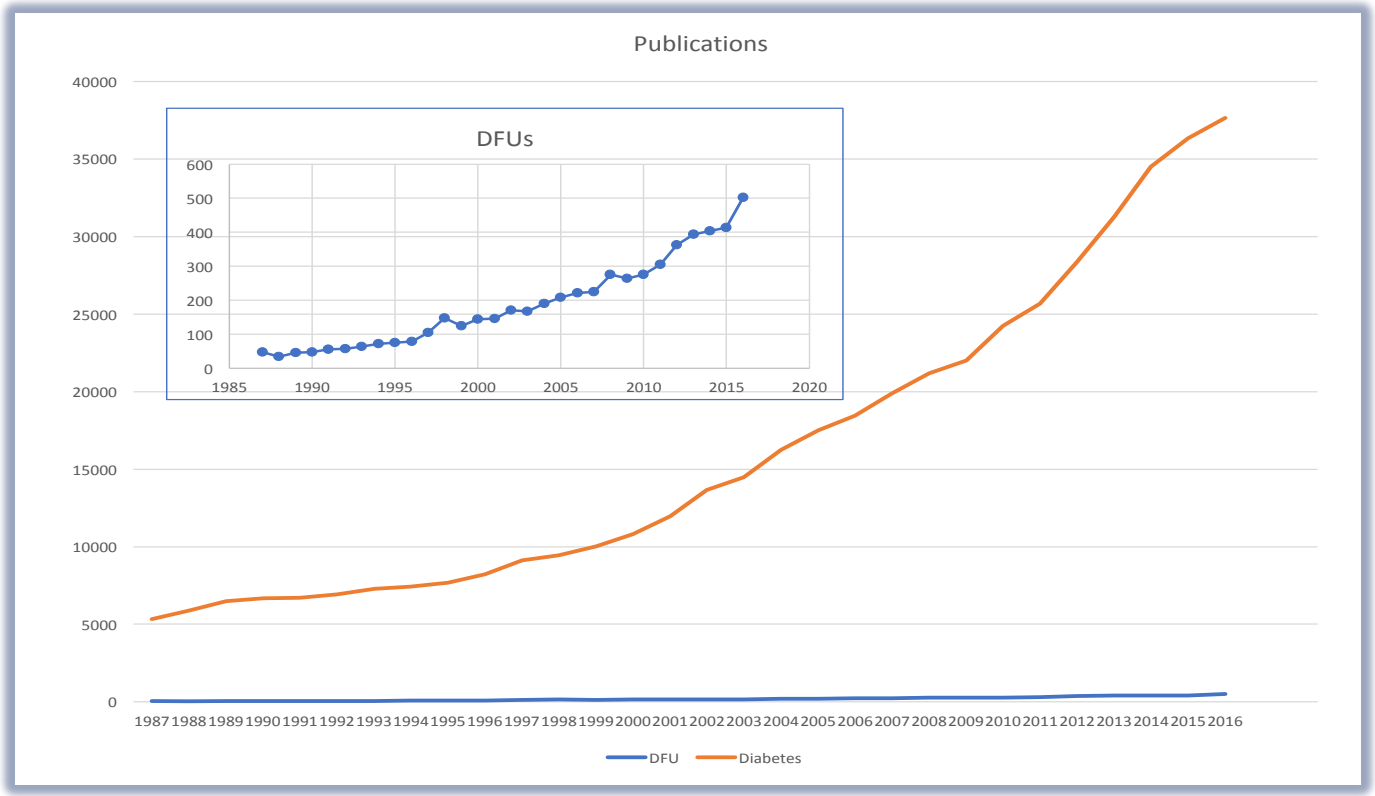
Kerr M 2017

How Do You Know What Works?

Hierarchy of Evidence



How Much Evidence is There?



What About Evidence in Foot Disease?

Diab Metab Res Rev, 2016 Suppl 1

The Last One - Effectiveness of Interventions to Enhance Healing of Chronic Ulcers of the Foot in Diabetes: a Systematic Review

Questions?

1. Debridement and wound bed preparation: sharp debridement, larvae

2. Wound bed preparation using antiseptics, applications and dressing products

3. Resection of the chronic wound

4. Oxygen and other gases

5. Compression or negative pressure wound therapy

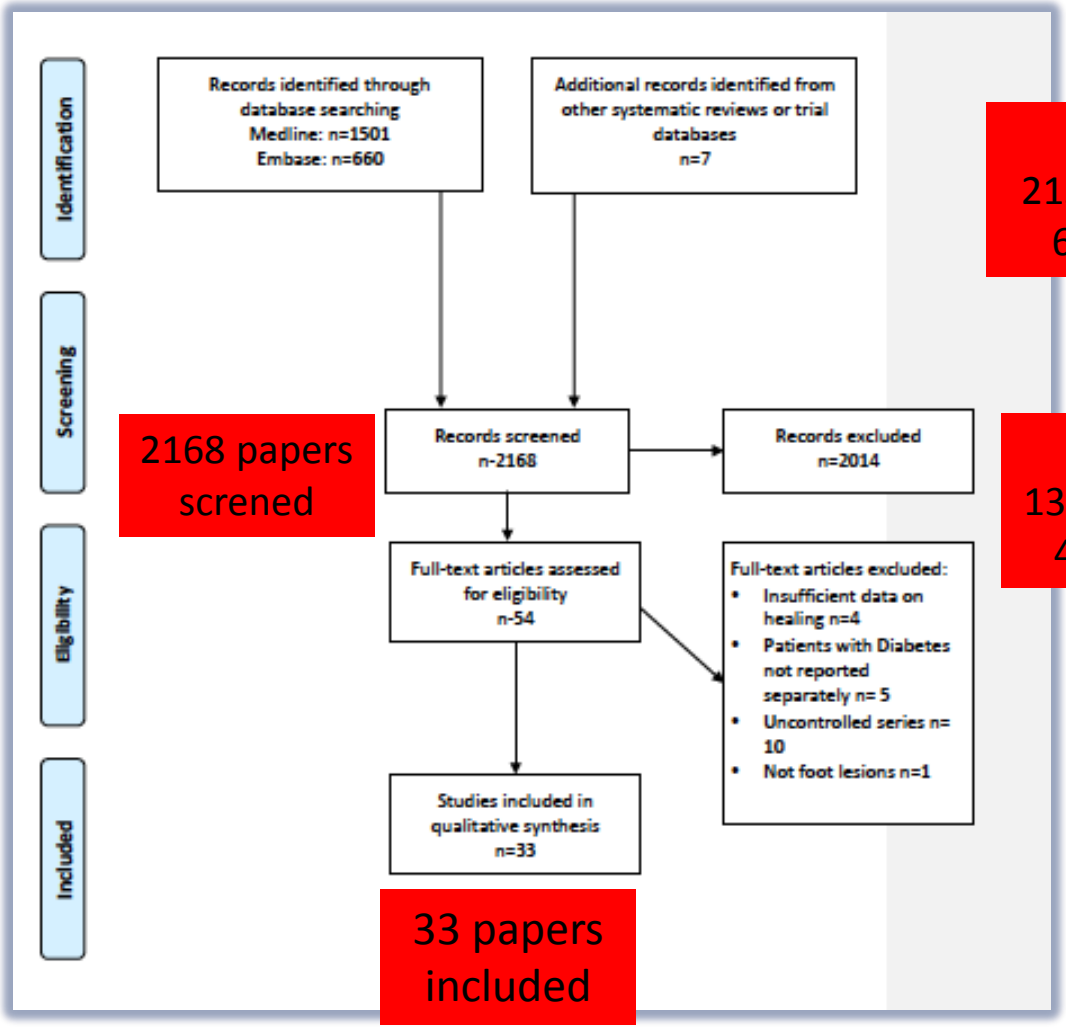
6. Products designed to correct aspects of wound biochemistry and cell biology associated with impaired wound healing

7. Application of cells, including platelets and stem cells, and growth factors

8. Bioengineered skin and skin grafts

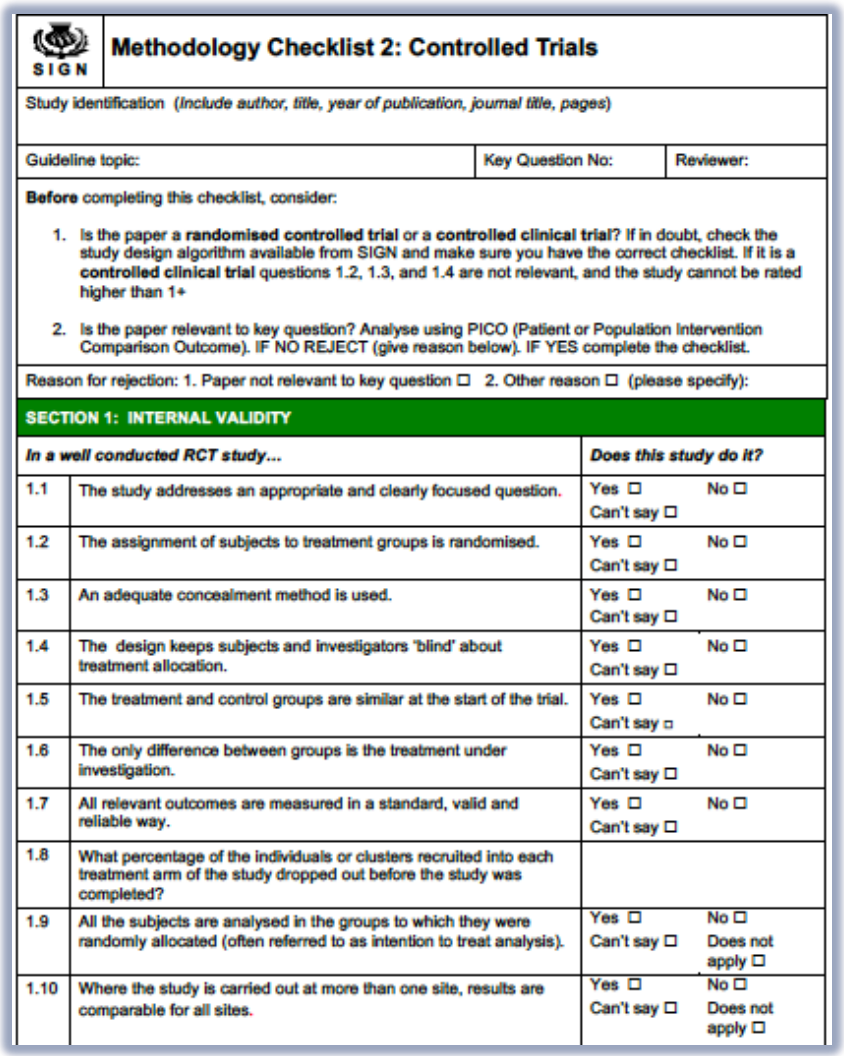
9. Electrical, electromagnetic, lasers, shockwaves and ultrasound

10. Other systemic therapies


Identification
Screening
Eligibility
Included
Records identified through database searching
Medline: n=1501
Embase: n=660
Additional records identified from other systematic reviews or trial databases
n=7
Records screened
n-2168
Records excluded
n=2014
Full-text articles assessed for eligibility
n-54
Full-text articles excluded:
Insufficient data on healing n=4
Patients with Diabetes not reported separately n= 5
Uncontrolled series n= 10
Not foot lesions n=1
Studies included in qualitative synthesis
n=33
2168 papers screned
33 papers included
2008
2155 identified
61 included
2012
1309 identified
43 included

Quality of Evidence

- “Overall low evidence base for the assessment of interventions: poor trial design and reporting”



SIGN

Methodology Checklist 2: Controlled Trials

Study identification (*Include author, title, year of publication, journal title, pages*)

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

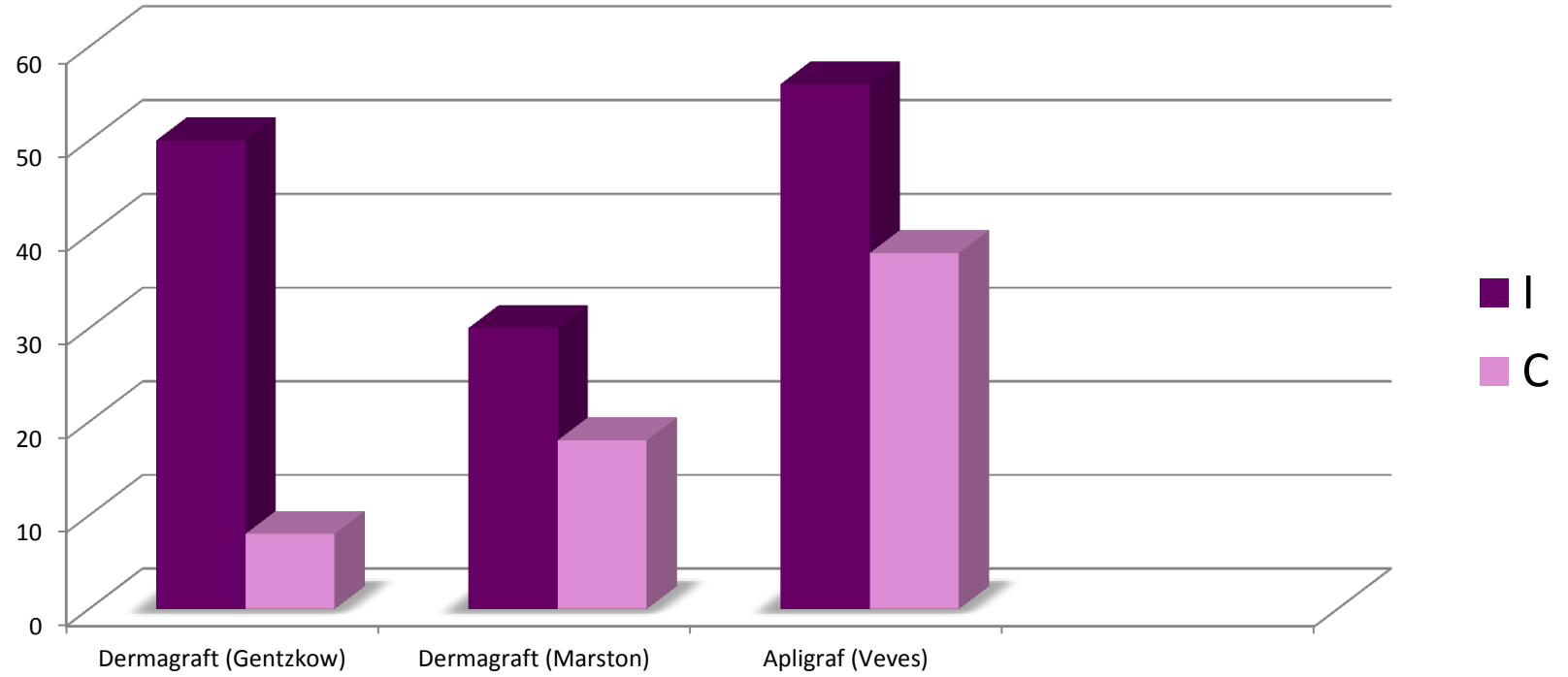
SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study...		*Does this study do it?*
1.1	The study addresses an appropriate and clearly focused question.	Yes ☐ No ☐ Can't say ☐
1.2	The assignment of subjects to treatment groups is randomised.	Yes ☐ No ☐ Can't say ☐
1.3	An adequate concealment method is used.	Yes ☐ No ☐ Can't say ☐
1.4	The design keeps subjects and investigators 'blind' about treatment allocation.	Yes ☐ No ☐ Can't say ☐
1.5	The treatment and control groups are similar at the start of the trial.	Yes ☐ No ☐ Can't say ☐
1.6	The only difference between groups is the treatment under investigation.	Yes ☐ No ☐ Can't say ☐
1.7	All relevant outcomes are measured in a standard, valid and reliable way.	Yes ☐ No ☐ Can't say ☐
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).	Yes ☐ No ☐ Can't say ☐ Does not apply ☐
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Yes ☐ No ☐ Can't say ☐ Does not apply ☐

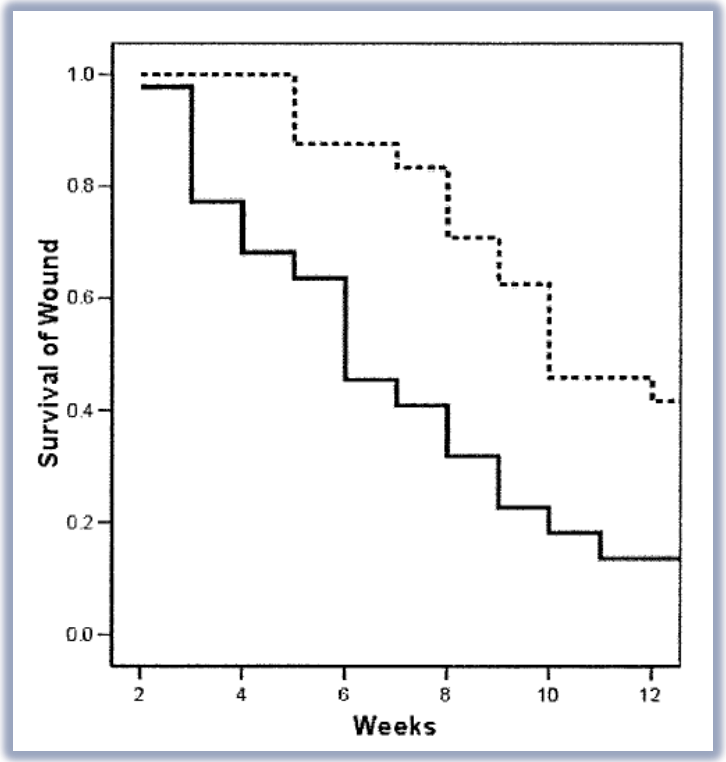
- **Only 25 studies were randomised**
- **Only 5 studies scored 6 or more**

SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise bias? *Code as follows:*	High quality (++)☐ Acceptable (+)☐ Low quality (-)☐ Unacceptable – reject 0 ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

Skin Substitute Studies

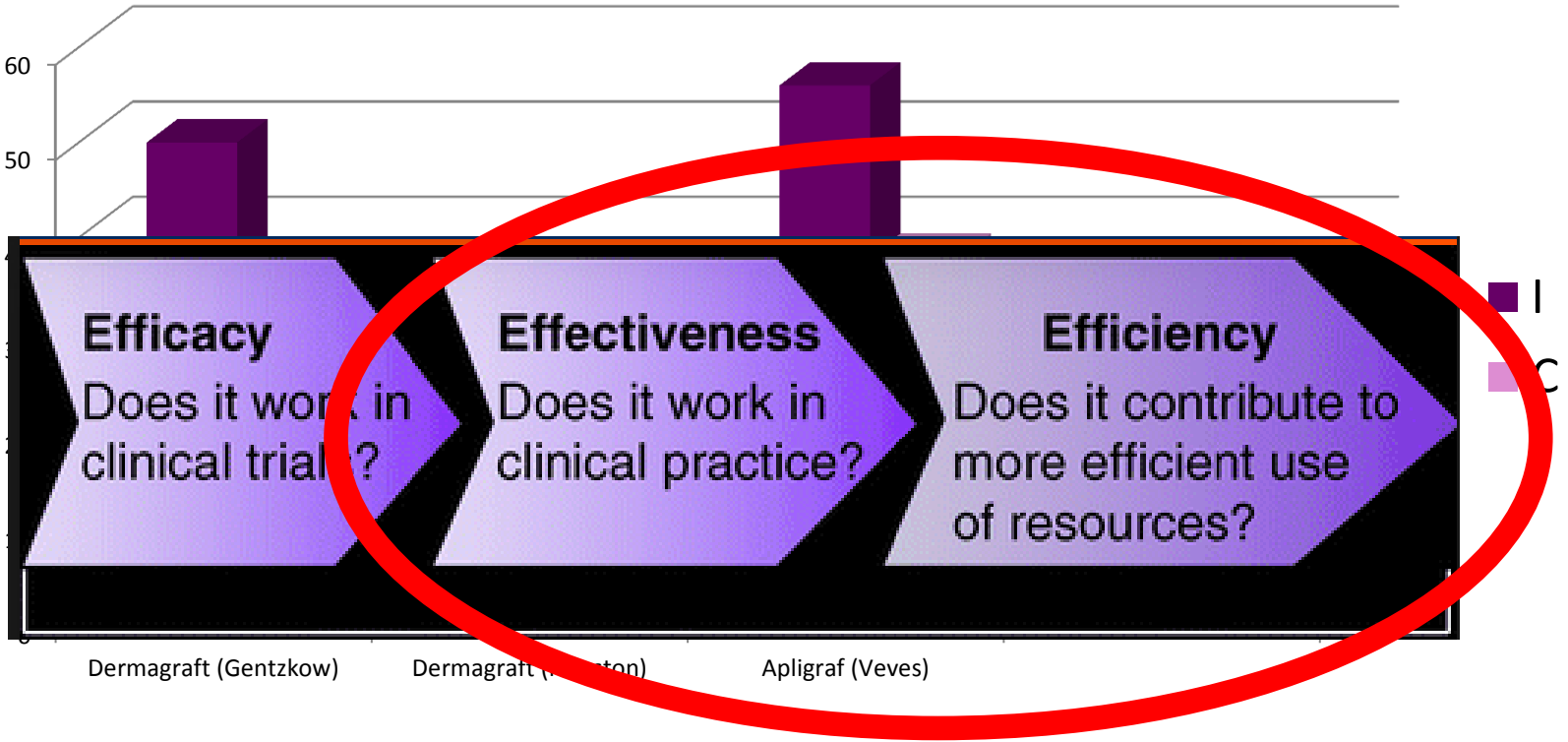


What Healing Rate is 'Standard of Care' Supposed to Achieve?

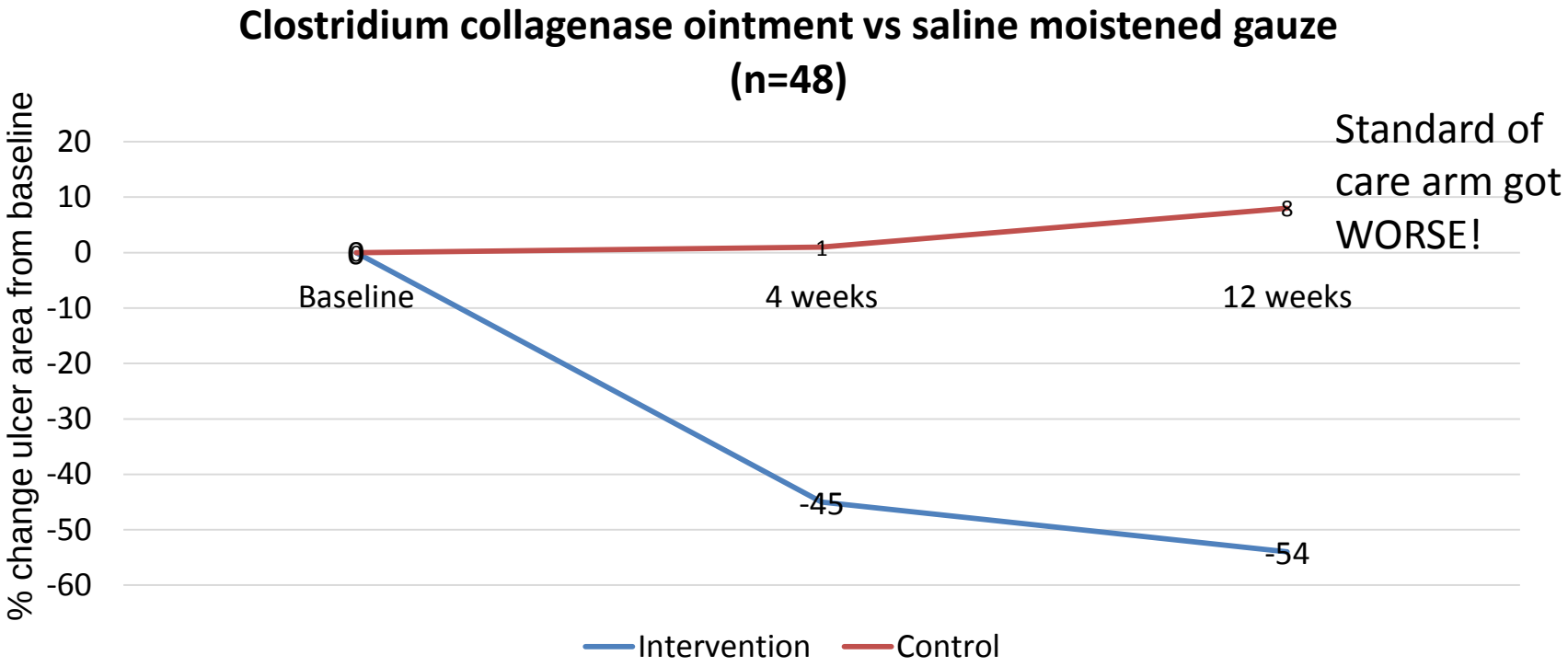


Armstrong DG et al Diabetes Care 2005;28(5):551-554

Skin Substitute Studies



Another Example



Tallis A Clin Therp 2013;35(11):1805-1820

To Help Everyone

Reporting standards of studies and papers on the prevention and management of foot ulcers in diabetes: required details and markers of good quality

William J Jeffcoate, Sicco A Bus, Frances L Game, Robert J Hinchliffe, Patricia E Price, Nicolaas C Schaper, on behalf of the International Working Group on the Diabetic Foot and the European Wound Management Association

The evidence base for many aspects of the management of foot ulcers in people with diabetes is weak, and good-quality research, especially relating to studies of direct relevance to routine clinical care, is needed. In this paper, we summarise the core details required in the planning and reporting of intervention studies in the prevention and management of diabetic foot ulcers, including studies that focus on off-loading, stimulation of wound healing, peripheral artery disease, and infection. We highlight aspects of trial design, conduct, and reporting that should be taken into account to minimise bias and improve quality. We also provide a 21-point checklist for researchers and for readers who assess the quality of published work.

Lancet Diabetes Endocrinol 2016; 4: 781–88

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Prevention, Management and Outcomes of Existing Ulcers

Population*
Person
Limb
Ulcer
Interventions

Prevention, Management and Outcomes of Existing Ulcers

Foot and limb

Person

Surrogate

Other Things that Need to be Reported

	Off-loading	Peripheral artery disease	Infections
Population	No additional details	• Smoking status • Ambulatory status • Previous interventions for peripheral artery disease • History of related disease (eg, coronary artery disease, heart failure, cerebrovascular disease) • Other relevant comorbidities (eg, renal disease, depression) • Relevant cardiovascular drugs • Limb symptoms: none, atypical (weakness or limping), intermittent claudication, and rest pain • Toe systolic pressure, toe-brachial pressure index, or $tcpO_2$ • Arterial pulse waveform • Anatomical distribution of the vascular disease in the leg • Number of active ulcers • Site of index ulcer	• Preceding antimicrobial use (type, route, duration, and time before presentation) • Immunosuppression • Infection type (using IDSA or PEDIS grading): none, mild, moderate, or severe • Involvement of bone or joint • Description of how samples were obtained for microbiological examination • Type of and results of microbiological examination (Gram stain and susceptibility)
Interventions	• Details on non-surgical device, application method, material use, and frequency of replacement • Specific design details of the foot–device interface • Person applying the device: the patient, a non-professional carer, or a health-care professional • Details of surgical intervention • Evidence of pressure-reducing efficacy if study is on plantar ulceration	No additional details	• Surgery undertaken before or in association with antimicrobial administration • Any other relevant intervention (including wound debridement, cleansing, and antiseptic use) undertaken before or in association with antimicrobial administration • Antimicrobial regimen: route of delivery, agents, and duration
Outcomes	• Ulcer healing • Adherence to the use of non-surgical removable interventions • Foot pressure (for footwear and surgical interventions) • Ambulatory activity level	• Number of participants alive with an intact foot • Description of outflow in the foot (in case of surgical or endovascular interventions) • Ulcer healing • Measures of the effectiveness of the vascular intervention (eg, toe pressures and $tcpO_2$) • Number of patients with minor and with major amputations	• Resolution of infection (which should be defined) at a prespecified time after stopping antimicrobial treatment • Clinical or laboratory signs of persistent infection at the end of antimicrobial treatment • Number and type of surgical procedures, including amputation (with level of amputation defined according to existing guidelines) • Days of antimicrobial use, antimicrobial-free days, and days of hospital admission • Prevalence of antimicrobial resistance after treatment

Jeffcoate WJ et al Lancet Diab Endo 2016;4:781-788

The 21-Point Checklist

Study design

1 Are appropriate definitions included for the terms "ulcer", "healing", and all other required aspects of the population and the outcomes?
2 Was the choice of study population appropriate for the chosen intervention and the stated conclusions?
3 Was there a control population that was managed at the same time as those in the intervention group or groups?
4 Is the intervention sufficiently well described to enable another researcher to replicate the study?
5 Are the components of other aspects of care described for the intervention and comparator groups?
6 Were the participants randomised into intervention and comparator groups?
7 Were the participants randomised by an independent person or agency?
8 Was the number of participants studied in the trial based on an appropriate sample size calculation?
9 Was the chosen primary outcome of direct clinical relevance?
10 Was the person who assessed the primary outcome or outcomes blinded to group allocation?
11 Were either the clinical researcher who cared for the wound at research visits or the participants blinded to group allocation?

Jeffcoate WJ et al Lancet Diab Endo 2016;4:781-788

The 21-Point Checklist

Study conduct

12 Did the study complete recruitment?
13 Was it possible to document the primary outcome in 75% or more of those recruited?
14 Were the results analysed primarily by intention-to-treat analysis?
15 Were appropriate statistical methods used throughout?

Outcomes

16 Was the performance in the control group of the order that would be expected in routine clinical practice?
17 Are the results from all participating centres comparable? Answer "yes" if the study was done in only one centre.

Study reporting

18 Is the report free from errors of reporting—eg, discrepancies between data reported in different parts of the report?
19 Are the important strengths and weaknesses of the study discussed in a balanced way?
20 Are the conclusions supported by the findings?
21 Is the report free from any suggestion that the analysis or the conclusions could have been substantially influenced by people with commercial or other personal interests in the findings?

Jeffcoate WJ et al Lancet Diab Endo 2016;4:781-788

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NHS Foundation Trust

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